REMARKS

Claims 1-24 are pending. Claim 16 is under examination. Claims 1-15 and 18-24 have been cancelled. Claim 16 has been amended. New claims 25 and 26 have been added. Support for the amendments and new claims can be found throughout the specification and the claims as filed. In particular, claim 16 has been rewritten in independent form, and support for the amendment to claim 16 can be found, for example, in original claim 15. Support for new claims 25 and 26 can be found, for example, in original claim 16. Accordingly, these amendments and new claims do not raise an issue of new matter and entry thereof is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claim 16 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite is respectfully traversed. Applicants have amended claim 16 to delete the term "synpasin-like protein," thereby rendering this rejection moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 112, First Paragraph

The rejection of claim 16 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed. Without addressing the merits of the rejection, Applicants have amended claim 16 to delete the term "synapsin-like protein" without prejudice to Applicants pursuing this subject matter in a related application. Accordingly, Applicants respectfully submit that this rejection has been rendered moot and respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

The rejection of claim 16 under 35 U.S.C. § 103 as allegedly obvious over Koutnikova et al., U.S. publication 2002/0155577, is respectfully traversed. Applicants respectfully submit that the claimed method is unobvious over Koutnikova et al.

Applicants respectfully submit that Koutnikova et al. does not teach or suggest Applicants' claimed methods. In the Office Action on page 4, it is acknowledged that Koutnikova et al. does not explicitly disclose using synaptotagmins as a substitute for PAP1.

Koutnikova et al. is asserted to disclose "that PAP1 protein shows a certain homology with various members of the synaptotagmin family," referring to paragraphs [0010, 0176 and 0178-0179]. It is further asserted in the Office Action that "[I]t would have been obvious to one of ordinary skill in the art at the time of the invention to try to substitute a synaptotagmin family member for PAP1 in a screening assay because PAP1, 'which is related to the synaptotagmins, shows no significant homology with known proteins, and can be used in therapeutic or diagnostic applications, for producing antibodies, probes or peptides, or for screening molecules' (paragraph [0178])." While Koutnikova et al. describes PAP1 as having homology with various members of the synaptotagmin family, the homology is quite low.

> [0176] Comparison of the sequence of this insert with the sequences which are contained in the GENBank and EMBL (European Molecular Biology Lab) databases showed a homology of 25% at the protein level with various members of the synaptotagmin family. The synaptotagmins are part of a family of membrane proteins which are encoded by at least eleven different genes, which are expressed in the brain and other tissues. They contain a single transmembrane domain and two calcium-regulated domains which are termed C_2. It is in this domain that the homology between the synaptotagmins and the PAP1 protein is found. No other significant homology was observed.
>
> [0178] These results thus show the existence of a novel protein, referred to as PAP1, which is capable of interacting specifically with parkin. This protein, which is related to the synaptotagmins, **shows no significant homology with known proteins**, and can be used in therapeutic or diagnostic applications, for producing antibodies, probes or peptides, or for screening active molecules.
>
> [0179] In order to identify the complete sequence of the human PAP1 gene and characterize the existence of variant forms, two elongation approaches were carried out from the sequence SEQ ID NO: 1. Two sequences were thus obtained, of 1644 bp and 1646 bp respectively, comprising an elongation of 330 bp as compared to the sequence SEQ ID NO: 1. Nonetheless, analysis of these sequences showed differences in the consensus region, which were apparent after translation. Thus an ORF of 420 aa is obtained in one case and an ORF of 230 aa with the other sequence. The protein sequence obtained was compared with the known sequences and revealed a 24% homology over the 293 amino acids that overlap with the human synaptogamin 1 (p65)(p21579).
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> Koutnikova et al., emphasis added.

Although PAP 1 is identified in Koutnikova et al. as having homology with synaptogamin, the homology is low, around 25% identity at the protein level. Furthermore,

Koutnikova et al. explicitly state that PAP1 "shows no significant homology with known proteins." Therefore, Applicants respectfully disagree with the assertion in the Office Action on page 4 that it would have been obvious to one skilled in the art "to try to substitute a synaptotagmin family member for PAP1 in a screening assay." To the contrary, given the low homology (25%) and the description that PAP1 showed "no significant homology with known proteins," one skilled in the art would not have viewed it to be obvious to modify the teachings of Koutnikova et al. and substitute a synaptotagmin for PAP1.

The rationale of obviousness set forth in the Office Action on page 4 is substitution of one known element for a similar known element to provide the same function. As stated in MPEP § 2143, four factors must be articulated to reject a claim based on this rationale: (1) a finding that the prior art contained a device (method, product, etc.) which differed from the claimed device by the substitution of some components (step, element, etc.) with other components; (2) a finding that the substituted components and their functions were known in the art; (3) a finding that one of ordinary skill in the art could have substituted one known element for another, and the results of the substitution would have been predictable; and (4) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness. First, Applicants respectfully submit that the substitution of a synaptotagmin for PAP1 would not have been obvious to one skilled in the art as being a substitution of a component, PAP1, with a component having a function known in the art, synaptotagmin, given that the homology between PAP1 and synaptotagmins was low, around 25%, and that it was not known that synaptotagmins could bind to parkin. Second, one skilled in the art would certainly have had no ability to predict, even if a synaptotagmin was substituted for PAP1, that such a substitution would yield predictable results again given the low homology and lack of knowledge that a synaptotagmin could bind to parkin. Therefore, Applicants respectfully submit that an adequate rationale that one skilled in the art would simply be substituting a known element by using a synaptotagmin instead of PAP1 has not been presented. Accordingly, Applicants respectfully submit that a *prima facie* case of obviousness has not been established.

Applicants respectfully submit that the claimed methods are unobvious over Koutnikova et al. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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